ABSTRACT

NQO1 is involved in the reductive bioactivation of cytotoxic antitumor quinone compounds, but also plays a protective role against the carcinogenicity and mutagenicity of quinones, their precursors and metabolites. One allele that predicts the function of this enzyme, NQO1*2, has been identified. Three forms of this allele exist, a functional allele, a nonfunctional allele, and an allele associated with diminished activity. The purpose of this study was to characterize interethnic variability in the frequency of the NQO1*2 nonfunctional allele in the Confederated Salish & Kootenai (CSK) population. One-hundred and twenty-five blood samples were tested for the allele by isolating the DNA from peripheral blood, performing PCR, digesting with restriction enzymes, and then analyzing the DNA fragments on a 1.5% agarose electrophoresis gel. The data analysis showed an elevated frequency of the nonfunctional allele in Native Americans when compared to Caucasian populations. The frequency of the variant in NQO1*2 is 16% in Caucasians as established in previous studies. As the blood quantum of the CSK blood samples approached 100%, the variant allele frequency approached 36%. Our data suggests that CSK population is at an increased risk of cancer due to a higher frequency of defective NQO1 enzyme. The higher allele frequency present in CSK members would also make genetic testing for the variant allele necessary before treatment with quinone based cancer therapies.

EXPERIMENTAL APPROACH AND METHODS

DNA was isolated from the blood samples using a Qiagen kit and diluted to 10ng/µL solutions. The polymorphic alleles of the human NQO2 promoter samples were amplified from the DNA samples using polymerase chain reaction (PCR) as in Gaedigk et al. Twenty nanograms of genomic DNA were used as the template.

The PCR products were digested with Hinf1 and incubated for three hours at 37°C before being separated in the gel.

PCR products were resolved on a 1.5% agarose-ethidium bromide gel in 0.5 X Tris-borate-EDTA buffer and photographed under UV light. Electrophoresis was carried out at 100V for two hours at room temperature.

RESULTS & CONCLUSION

◆ As the blood quantum samples approached 100% the variant allele frequency approached 36%. This number is more than twice as large as the Caucasian NQO1*2 frequency.
◆ This allele frequency is crucial for helping doctors correctly prescribe medication to CSK patients, avoiding unnecessary and sometimes fatal ADRs.
◆ This data could help explain the elevated rate of certain cancers in American Indian populations.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Ratio(NA/NHW)</th>
<th>Wild Type</th>
<th>Variant</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1.17</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>3.97</td>
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<td>36%</td>
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<tr>
<td>Liver</td>
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<tr>
<td>Penis</td>
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<td>46%</td>
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<tr>
<td>Stomach</td>
<td>2.21</td>
<td>51%</td>
<td>49%</td>
</tr>
</tbody>
</table>

NQO1*2 Allele Frequencies in Selected Ethnicities (1)

Acknowledgments

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REFERENCES